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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/765,324	12/24/96	KOREN E	OMRF143-CIP2

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EXAMINER	
DUFFY,P	
ART UNIT	**PAPER NUMBER**
1645	14

DATE MAILED: 05/26/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
08/765,324	Koren
Examiner	**Group Art Unit**
Duffy	1645

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- [x] Responsive to communication(s) filed on Amendment of 2-26-97.
- [x] This action is **FINAL.**
- [ ] Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- [x] Claim(s) 15, 16, 18, 20-23, 25, 27-30, 35-37, 41+42 is/are pending in the application.
- Of the above claim(s) _____ is/are withdrawn from consideration.
- [x] Claim(s) 35-37 is/are allowed.
- [x] Claim(s) 15, 16, 18, 20, 23, 25, 27-30, 41+42 is/are rejected.
- [x] Claim(s) 21 and 22 is/are objected to.
- [ ] Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- [ ] See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- [ ] The proposed drawing correction, filed on _____ is [ ] approved [ ] disapproved.
- [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.
- [ ] The specification is objected to by the Examiner.
- [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- [ ] Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
  - [ ] All [ ] Some* [ ] None of the CERTIFIED copies of the priority documents have been
  - [ ] received.
  - [ ] received in Application No. (Series Code/Serial Number) _____.
  - [ ] received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Attachment(s)

- [ ] Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- [ ] Interview Summary, PTO-413
- [ ] Notice of Reference(s) Cited, PTO-892
- [ ] Notice of Informal Patent Application, PTO-152
- [ ] Notice of Draftsperson's Patent Drawing Review, PTO-948
- [ ] Other _____

Office Action Summary

Response to Amendment

1. The amendment filed 2-26-99 has been entered into the record. Claims 15, 16, 18, 20-23, 25, 27-30, 35-37 and 41-42 are pending and under examination.

2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Maintained

3. The rejection of claims 16 and 42 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained in part and overcome in part is maintained for reasons made of record for claims 15-18, 20-23, 25, 27-30, 35-37, 42 and 45-47 in Paper No. 11, mailed 10-28-98.

As to claims 16 and 42, the amendment to the claims fails to obviate the outstanding rejection. The claims are still missing essential steps which are required to be able to specifically detect the instantly claimed fractions.

As to claim 16, the claim is still not enabled because both antibodies are added to "the sample" and thus even the separation step is insufficient to obviate this rejection because it is unclear how the now recited separation step determines the amount of VLDL and HDL in the sample because all the antibodies are added to the same sample. It appears that applicants should recite that the antibodies are added to a first and second aliquot of the same sample, but not the identical sample, otherwise there is no way the assay could work unless the antibodies were separately immobilized.

As to claim 42, the function of these assay requires that the antibodies be immobilized in order to function to separate the indicated fraction otherwise both antibodies are added to the same sample and the claim does not provide for a method which distinguishes between the two lipoproteins. Absent immobilization of the antibodies which bind non-cross reactive lipoprotein antibodies, the assay will not specifically detect the claimed fractions and thus, will not work. This similar reasoning was applied to claims 16 and 42. In the absence of further guidance from applicants and that the specification requires that particular antibodies must be immobilized for the assay to operate, it would require undue experimentation on the part of the skilled artisan to make and use the assay as instantly claimed and the claims should be so limited is maintained for reasons made of record.

Applicants' amendment and remarks have been carefully considered but are insufficient to overcome the rejection because the claims fail to indicate that the lipoprotein particles *the particles which bind both APO C-III and pan B must be separated from the lipoprotein mixture.* Currently, the claims recite "the complexed antibody-lipoprotein particles", and proper antecedent basis for the term resides in the first complex formation (i.e. APO-CIII containing lipoprotein particles). The separation must include the Pan B antibody. Currently the Pan B antibody is contacted to the biological sample and not the complex formed by the antibody of the Apo C-III and the Apo C-III containing lipoprotein, if both are not separated then one skilled in the art could not determine the amount of Apo C-III associated with Apo B in the same lipoprotein particle. Applicants assert that claim 17 does not need a separation step, this is not persuasive because it is not apparent how a ratio is determined in the absence of such a step. Clarification is requested.

4. The rejection of claims 15, 16, 30, 41, and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons made of record in Paper No. 11, mailed 10-20-98.

As to method claims 15, 16, 41 and 42, the claims remain confusing as to when each antibody is being added wether the antibodies are added together or separate or if the sample is separated into two aliquot or processed in the same sample. Applicants' recitation of "separate sample" is not clear that the processing is done on separate aliquots of the same biological sample. The amendments to claim 16 are highly confusing because it is not clear what antibodies are added to when. Is the VLDL analyzed using the supernatant of the HDL immunoprecipitate or is it paralleled processed in a separate aliquot of the same biological sample. Clarification is requested.

As to claim 30, the claim still remains confusing because the terms lack antecedent basis in the independent claim 18. It is noted that applicants have amended claims 28 and 29 appropriately. The examiner suggests that a similar amendment to this claim would obviate this rejection. The amendment is insufficient to obviate the rejection because Apo A-I lacks basis in claim 18. Applicants should amend the claim to recite "further comprising" to obviate this rejection.

5. The rejection of claims 18, 20, 27, 28 and 29 under 35 U.S.C. 102(b) as being anticipated by Koren et al (Biochimica et Biophysica Acta, 876:91-100, 1986; herein after called Koren AR) or Koren et al (Biochimica et Biophysica Acta, 876:101-107, 1986; herein after called Koren AS) is maintained for reasons made of record in Paper No. 11, mailed 10-20-98.

Applicants' arguments have been carefully considered but are not persuasive. Applicants' argue that the D6 antibody is not specifically reactive with a particular lipoprotein. This is not persuasive, the claims alternatively encompass an antibody which binds a particular apolipoprotein in view of the recited "or" in the claims. Thus, the claims are not limited to a single lipoprotein, as argued by applicants, but also encompass a monoclonal antibody which binds a single apolipoprotein (e.g. Apo B). The D6 antibody specifically binds the single apolipoprotein B, the epitope of which as previously set forth, is stable and is uninfluenced by lipid content. The single lipoprotein (e.g. particle VLDL, LDL, HDL) argued by applicants is recited in the alternative (i.e. the instant "or") to an apolipoprotein (Apo A-I, Apo A-II, Apo B, Apo C-III or Apo E). Thus, applicants' arguments are not commensurate in scope with the claims and the claims as amended do not distinguish over the prior art.

6. The rejection of claims 18, 20, 23, 25, 27, 28, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koren et al (Biochimica et Biophysica Acta, 876:91-100, 1986; herein after called Koren AR) or Koren et al (Biochimica et Biophysica Acta, 876:101-107, 1986; herein after called Koren AS) as applied to claims 18, 20, 23, 25, 27, 28, 29 and 35 above, and further in view of Koren et al (Atherosclerosis, 95:157-170, 1992; herein after referred to as Koren A) is maintained for reasons made of record in Paper No. 11, mailed 10-20-98.

Applicants' arguments have been carefully considered but are not persuasive. Applicants' argue that since Koren AS and Koren AR fail because the D6 antibody is not specifically reactive with a particular lipoprotein or apoliproprotein and Koren A does not fulfill this deficiency. This is not persuasive, the claims alternatively encompass an antibody which binds a particular apolipoprotein in view of the recited "or" in the claims and thus still read on Koren AS and Koren AR. Thus, the claims are not limited to a single lipoprotein, as argued by applicants,

but also encompass a monoclonal antibody which binds a single apolipoprotein (e.g. Apo B). The D6 antibody specifically binds the single apolipoprotein B, the epitope of which as previously set forth, is stable and is uninfluenced by lipid content. The single lipoprotein (e.g. particle VLDL, LDL, HDL) argued by applicants is recited in the alternative (i.e. the instant "or") to an apolipoprotein (Apo A-I, Apo A-II, Apo B, Apo C-III or Apo E). Thus, applicants arguments are not commensurate in scope with the claims and the claims as amended do not distinguish over the prior art. Applicants argue that the D6 antibody is not specific for a single apolipoprotein. This is not persuasive in view of the teachings of Koren AS and Koren AR which specifically teach that the D6 antibody is specific for apolipoprotein B. Applicants argue the combination of the two limitations whereas the claims recite them in the alternative.

7. The rejection of claims 18, 20 and 27 are rejected under 35 U.S.C. § 102(b) as being anticipated by Marcel et al (J Lipid Res, 28(7):768-77, 1987) is maintained for reasons made of record in Paper No. 11, mailed 10-20-98.

Applicants' arguments have been carefully considered but are not persuasive. Applicants' argue that Marcel et al fails because it is not specific for a single lipoprotein. This is not persuasive, Apo A-I is only present in HDL lipoprotein particles and thus the monoclonal antibody of Marcel is specific for a single lipoprotein. Additionally, applicants' arguments are not persuasive, the claims alternatively encompass an antibody which binds a particular apolipoprotein in view of the recited "or" in the claims and thus still read on Marcel et al which teach an antibody which binds a stable conformational epitope and ApoA-I which is uninfluenced by storage. The single lipoprotein (e.g. particle VLDL, LDL, HDL) argued by applicants is recited in the alternative (i.e. the instant "or") to an apolipoprotein (Apo A-I, Apo A-II, Apo B, Apo C-III or Apo E). Thus, applicants arguments are not commensurate in scope with the claims and the

claims as amended do not distinguish over the prior art. Applicants appear to argue the combination of the two limitations whereas the claims recite them in the alternative.

8. The rejection of claims 18, 20, 23, 25, 27, 28, 29, and 30 under 35 U.S.C. 103(a) as being unpatentable over Marcel et al (J Lipid Res, 28(7):768-77, 1987). as applied to claims 18, 20, 27 and 35 above and further in view of Koren et al (Atherosclerosis, 95:157-170, 1992; herein after referred to as Koren A) is maintained for reasons made of record in Paper No. 11, mailed 10-20-98.

Applicants argue that since Marcel et al fails, so does the 103 based on Marcel et al since Koren A does not rectify the deficiencies of Marcel et al. This is not persuasive because a Apo AI is only present in HDL and thus it innately binds a single lipoprotein particle. Alternatively, the claims also encompass an antibody which binds a particular apolipoprotein in view of the recited "or" in the claims and thus still read on Marcel et al. Thus, for the foregoing reasons Marcel et al does not fail and the rejection is maintained.

New Rejections Based on Amendment

9. Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 41, the claim is rendered indefinite from the recitation of "the second antibody" ant "the antibody:lipoprotein complex" both lack antecedent basis in claim 15.

Status of Claims

10. Claims 21, 22 are objected to as depending from rejected base claims. All other claims stand rejected. Claims 35-37 are allowed. Claims 15, 16, 18, 20, 23, 25, 27-30, 41 and 42 are rejected.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (703) 308-3995.

Patricia A. Duffy, Ph.D.
May 24, 1999

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600